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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,801	09/17/2003	Torben Halkier	4614-0120P	3913

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

NOTIFICATION DATE	DELIVERY MODE
05/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/664,801	HALKIER ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58,59,61,62 and 67-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58,59,61,62 and 67-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 October 2007 has been entered.

Status of Application, Amendments and/or Claims

The amendment filed 29 October 2007 has been entered in full. Claims 1-57, 60, 63-66 are canceled. New claim 75 was entered. Claims 58, 59, 61, 62, 67-75 are pending and under examination.

Withdrawn Objections And/Or Rejections

The rejection to claims 58, 59, 61, 67, 69, 70, 72 and 73 under 35 U.S.C. 112, first paragraph, scope of enablement, as set forth at pages 2-5 of the previous Office Action (27 June 2007), is *withdrawn* in view of the new rejections set forth below.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 58, 59, 61, 62, 67-71, 73, 74 (and new claim 75) remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 7 and 15 of U.S. Patent No. 6,645,500 B1 in view of Tsukii et al. (reference of record, Biochemical and Biophysical Research Communications 246:337-341; 1998). The basis for this rejection is set forth at pages 6-7 of the previous Office Action (27 June 2007).

The claims of U.S. Patent No. 6,645,500 B1 are drawn to a method for *in vivo* down-regulation of osteoprotegerin ligand (OPGL) activity in an animal comprising effecting presentation to the animal's immune system of an immunogenically effective amount of at least one OPGL polypeptide or analogue thereof which has a result that immunization of the animal with the OPGL polypeptide or analogue thereof, induces production of antibodies against the animal's own OPGL polypeptide which down-

regulates the animal's own OPGL activity, wherein said OPGL polypeptide or analogue thereof comprises the sequence of residues 159-317 of SEQ ID NO:2 or the sequence of residues 159-317 of SEQ ID NO:2 wherein at least one foreign promiscuous, immunodominant T helper lymphocyte epitope (Th), is introduced in said residues 159-317. The claims of U.S. Patent No. 6,645,500 B1 also teach adjuvants.

Although the conflicting claims are not identical, they are not patentably distinct from each other. The OPGL polypeptide or analogue thereof (species claim) administered to down-regulate an animal's own OPGL activity in US Patent 6,645,500 B1 is encompassed by the immunogenic agent administered to down-regulate autologous OPGL (genus claim) of the instant application. The species renders the genus obvious. The claims of U.S. Patent No. 6,645,500 B1 do not teach treating/ameliorating a disease characterized by excessive bone resorption.

Tsukii et al. teach osteoclast differentiation factor (ODF) as being identical to RANKL/OPGL (page 337, 2nd paragraph). Tsukii et al. teach that OPG inhibits osteoclast development (inhibits resorption) *in vivo* (page 337, 1st-2nd paragraph). Tsukii et al. teach that *in vitro* bone resorption assays based on a bone tissue culture provides a system similar to the *in vivo* tissue microenvironment (page 338, 1st paragraph). Tsukii et al. teach that ODF induced bone resorption in fetal mouse long bone and antibodies against ODF suppressed bone resorption induced by various factors (page 339, Discussion).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of U.S. Patent 6,645,500 B1 by formulating it

for down-regulation of autologous OPGL or treating/ameliorating disease in an individual characterized by excessive bone resorption comprising administering an immunogenic agent capable of inducing an immune response (or an antibody response) against the subject's autologous OPGL. One having ordinary skill in the art would have been motivated to make such modifications because U.S. Patent 6,645,500 B1 teach the down-regulation of OPGL activity comprising administering an OPGL polypeptide or analogue thereof to induce production of antibodies against the subjects own OPGL. Tsukii et al. teach that ODF (i.e. RANKL/OPGL) induced bone resorption in fetal mouse long bone and antibodies against ODF suppressed bone resorption.

Applicant states that this rejection will be addressed upon a finding of patentable subject matter (16 April 2007; page 13). The rejection is still maintained for reasons of record.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58, 59, 61, 67, 69, 70, 72, 73 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

application was filed, had possession of the claimed invention. The basis for this rejection is set forth at pages 5-6 of the previous Office Action (27 June 2007).

Applicant submits that the present claims in their present form meet all statutory patentability requirements, at least for the reasons of record. Applicant states that they intend to file declarations by persons of ordinary skill in the art, supporting the facts that the present claims meet the written description requirements.

Applicant's arguments have been fully considered but are not deemed persuasive. Applicant is reminded of the revision to the Written Description Training Materials, created on March 25, 2008, to supersede and replace the 1999 training materials (www.uspto.gov/web/menu/written.pdf). Due to limited guidance in the specification, the Examiner has interpreted the term "an immunogenic agent" to encompass, lipids, antibodies, nucleic acids, chemical analogs, biomolecules, macromolecules, etc. The instant claims also recite that the "immunogenic agent" can be a "peptide immunogen", a "nucleic acid immunogen" and/or "a non-pathogenic organism". The instant method requires the use of undisclosed agents. The specification fails to provide written support for this genus of molecules, which have the functions of effecting presentation to the immune system and inducing an immune response that cross react with OPGL in a subject, thus down-regulating the OPGL of said subject. Applicant was not in possession of the claimed "immunogenic agents" as an element of the claimed methods in the absence of providing sufficient structural and functional characteristics of the genus. The instant claims are not limited to a structure. There is insufficient written description as to those "immunogenic agents" that would be

applicable for administration in humans, as broadly encompassed. The specification does not describe the members of the genus by physical and/or chemical characteristics. Without a recognized correlation between structure and the function consistent with the claimed method, those of ordinary skill in the art would not be able to identify, without further testing, ***which*** agent (i.e. immunogenic agent, peptide immunogen, nucleic acid immunogen and/or a non-pathogenic organism) has the claimed function. The artisan would need to know which regions of the disclosed molecule are responsible for the interactions underlying its biological function(s). Common structural attributes of the species in the genus are not described in the specification. All members of the genus have the same function, (*i.e.,* effecting presentation to the immune system and inducing an immune response that cross react with OPGL in a subject, thus down-regulating the OPGL in subject), *but no correlation between the structure of the members of the genus and their common coding function is disclosed.* The specification fails to teach how the structure of any one of the immunogenic agents is representative of other unknown immunogenic agents having concordant or discordant functions. There is insufficient descriptive support because the instant claims are drawn to a genus of immunogenic agents based entirely on function (i.e. binds selectively a second protein encoded by..). One of skill in the art would conclude that the Applicant was not in possession of the claimed genus.

The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections-35 USC § 112, First Paragraph, Written Description, New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58, 59, 61, 62, 67-74 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.** The basis for this rejection is set forth at pages 7-9 of the previous Office Action (27 June 2007).

The specification as originally filed does not provide support for the invention as now claimed:

"autologous immunogenic" (claims 58, 59, 61, 62, 67)

"non-pathogenic organisms (claims 69 and 72)

"Streptococcus ssp." (claim 72)

"vaccine" (claim 72)

Applicant's amendment, filed 16 April 2007, asserts that no new matter has been added but does not provide sufficient direction for the written description for the above-mentioned limitation "autologous immunogenic". The Examiner cannot locate the wording or connotation of the instant claims.

Applicant directs support to pages 29, 36 and 39 for claim 69 and page 39 for claim 72. The Examiner has located the limitations "non-pathogenic **micro**organism" (page 39, lines 10-11), "**non-pathogenic** Steptococcus spp." (page 39, line 16) and vacci**nia** (page 39, line 27).

The specification as filed does not provide a written description or set forth the metes and bounds of this "limitations". The specification does not provide direction for the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as-filed. Applicant is required to cancel the new matter in the response to this Office action. Alternatively, Applicant is invited to provide specific written support for the "limitations" indicated above or rely upon the limitations set forth in the specification as filed.

The instant rejection was not addressed by Applicant. The rejection is still maintained for reasons of record.

NEW CLAIM REJECTIONS/OBJECTIONS

Claim Rejections-35 USC § 112, First Paragraph, Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 58, 59, 61, 62, 67-75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification states that that the invention provides a method for down-regulating osteoprotegerin ligand (OPGL) by enabling production of antibodies against OPGL suffering from or in danger of suffering from osteoporosis (page 1, lines 10-15 and page 8, lines 4-25). The specification teaches that OPGL is normally non-immunogenic when presented to the animal to be treated and will not normally give rise to an immune response against OPGL of the animal in question (page 10, lines 1-15). The specification states that the down-regulation can be obtained by several mechanisms: of these, simple interference with the active site in OPGL by antibody binding is the most simple. It is also within the scope of the invention that the antibody binding results in removal of OPGL by scavenger cells (such as macrophages and other phagocytic cells). The instant claims, as recited, are not enabled for the following reasons:

The invention is relying on the instant invention to mount a response against an endogenous protein. The art of using vaccines against self-proteins is a complicated and unpredictable art and various criteria must be met. It is known to those skilled in the art that overcoming autotolerance against an endogenous protein is very difficult. In fact, page 13, lines 3-14 of the specification teaches, "when discussing autotolerance towards OPGL, it is understood that since OPGL is a self-protein in the population to be vaccinated, normal individuals in the population do not mount an

immune response against OPGL..". "At any rate, an animal will normally only be autotolerant towards its own OPGL..". The specification fails to disclose examples demonstrating that upon administering an agent (i.e. immunogenic agent, peptide immunogen, nucleic acid immunogen, non-pathogenic organisms, OPGL polypeptide, SEQ ID NO:2 and a T-helper epitope) antibodies against endogenous OPGL are produced which result in *in vivo* down-regulation of endogenous OPGL activity. Pharmaceutical therapies in the absence of *in vivo* clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). Buckel points out the difficulties using proteins for treatment such as optimization and administering of proteins, solubility and possible side effects (see Buckel, Trends in Pharmacology Science, 1996 Vol. 450-456). The specification fails to disclose and/or teach any working examples. The instant vaccine must be designed to break immune tolerance and the specification fails to demonstrate that the claims, as recited, are enabled for this activity.

The instant claims, as recited, fail to teach specific foreign T-helper epitopes or positions in the OPGL molecule where foreign T-helper epitopes should be inserted. Hertz et al. (The Journal of Immunology, Vol. 167:3792-33799, 2001) teach active vaccination against IL-5 for treating asthma. Hertz et al. teach that immune responses against self-proteins such as IL-5 are usually not generated due to immunological tolerance. Hertz et al. teach that the introduction of promiscuous foreign Th epitopes break immunological tolerance to IL-5. Hertz et al. employ P30 from the tetanus toxoid (page 3797-3798). Indeed, page 15, lines 20-25 of the specification teaches that "the OPGL polypeptide should be modified, since the chances of breaking autotolerance towards OPGL are greatly facilitated that way". The specification teaches the introduction of foreign T-cell epitopes (page 16-17). Thus, the use of foreign T-helper epitopes is very important in when trying to break autotolerance. Page 21, lines 15-23 of the specification state, "it is a well-know fact that a T-cell epitope which is immunodominant in one individual/population, is not necessarily immunodominant in another individual of the same species, even though it may be capable of binding MHC-II molecules in the latter individual." "When selecting T-cell epitopes to be introduced in the OPGL analogue, it is important to include all knowledge of the epitopes which is available: 1) the frequency of responders in the population to each epitope, 2) MHC restriction data, and 3) frequency in the population of the relevant haplotypes". "There exists a number of naturally occurring promiscuous T-cell epitopes which are active in a large proportion of individuals of an animal species or an animal population and these are preferably introduced in the vaccine thereby reducing the need for a very large

number of different OPGL analogues in the same vaccine"(page 24, lines 8-13). The specification states that because of OPGL's structural relationship with TNF-α and other members of the tumor necrosis factor family, it is predicted that the introductions of T-cell epitopes in areas defined by positions 171-193, 199-219, 222-247, 257-262 and 286-317 will be most likely to produce the desired effect. These are positions in human OPGL, SEQ ID NO:2 (page 28, lines 23-33). The specification states that not all possible variants or modifications of native OPGL will have the ability to elicit antibodies in animals (page 51, lines 5-8). Selected positions for the introduction of variation (such as introduction of foreign T-helper epitopes) are chosen based on knowledge of existing B-cell epitopes and predicted secondary structure elements of the native molecule as well as using alignments and modeling (page 57, lines 21-31). The instant examples cite specific regions for insertion of specific foreign T-helper epitopes (P2 or P30) in the OPGL protein.

The specification fails to teach how to use a non-pathogenic organism such as vaccinia or pox virus comprising OPGL as a vaccine. It could not be predicted that the instant data presented in the specification would be in any way correlative with administration of non-pathogenic organism comprising OPGL. The Examiner submitted reference that teach the problems associated with the use of live bacterial carriers such as reversion to virulence, horizontal gene transfer, host genetic factor, immune responses, accommodation of heterologous DNA, safety concerns, lyophilization and/or host cell range of vaccine vectors. For example, Dudek et al. (reference of record, Virology, 344:230-239, 2006) teach that poxviruses are strong

candidates for vaccine vectors but concerns about their safety still remain. The quantity of experimentation for the instant invention is not routine and the specification has provided little guidance on how to make and/or use the instant invention in a safe and effective manner.

The specification fails to teach how to use any cytokine as an adjuvant. Barouch et al. (Immunological Reviews, Vol. 202:266-274, 2004) teach that a major limitation in the use of cytokines proteins as adjuvants, besides short *in vivo* half-life, is the potential for adverse effects. Barouch et al. teach that high-dose systemic administration of IL-2 has been associated wit numerous toxicities including severe capillary leak syndrome and that many investigators have chosen to develop plasmids expressing cytokine genes instead of utilizing purified cytokine proteins. Barouch et al. teach that large numbers of plasmid cytokines have been evaluated as DNA vaccine adjuvants in small animal models, but few have entered clinical trials to date (page 268, last paragraph-page 269, 1st paragraph). Other studies have underscored the complexities associated with augmentation of DNA vaccines. In contrast with its ability to augment cellular immune responses, plasmid IL-12 has been reported to suppress antibody responses to DNA vaccines in mice and primates. The dose and timing of plasmid IL-12 administration in relation to DNA vaccination appear to be critical in determining its adjuvant effects (page 269, last paragraph-page 270, 1st paragraph). Barouch et al. teach that the utility of these strategies in humans has not yet been determined (page 270, 2nd paragraph). Scientific challenges for advancing plasmid cytokines into clinical trial include the current inability to predict which preclinical

models, immunization parameters, and specific cytokines will translate successfully to humans (page 271, 5th paragraph). Thus, the quantity of experimentation for the instant invention is not routine and the specification has provided little guidance on how to make and/or use the instant invention in a safe and effective manner.

Claims 58, 59, 61, 67, 69, 70, 72 and 73 recite limitations "immunogenic agent", "peptide immunogen", "nucleic acid immunogen" and/or "a non-pathogenic organism" and the specification fails to teach what structural limitations are required for the claimed activity. The instant claims fail to recite structural limitations, to encompass any immunogenic agent. The specification fails to teach how to make and use "any immunogenic agent" to induce an immune response, cross react and down-regulate autologous OPGL in an individual. The instant specification fails to indicate that a representative number of structurally related compounds are disclosed and therefore, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claim and would not know how to make them. Without a recognized correlation between structure and the function consistent with the claimed method, those of ordinary skill in the art would not be able to make/use, without further testing, *which* agent (i.e. immunogenic agent, peptide immunogen, nucleic acid immunogen and/or a non-pathogenic organism) has the claimed function. The artisan would accordingly have no resort save trial-and-error experimentation to determine which of the astronomically large number of possible structural molecules had the functional properties of the claimed immunogenic agent. In addition, the specification fails to disclose examples

demonstrating that upon administering *any immunogenic agent*, antibodies against the immunogenic agent will result in *in vivo* down-regulation of ONLY endogenous OPGL activity. The immunogenic agent should ONLY recognize endogenous OPGL to induce an immune response. Any immunogenic agent, capable of inducing an immune response against the subject's self-OPGL, could potentially down-regulate other autologous proteins in an individual.

Due to the large quantity of experimentation necessary to induce an immune response that cross reacts with OPGL in a subject and thereby down-regulate the OPGL in said subject without introducing specific foreign T-helper epitopes in specific positions in the OPGL molecule, the large quantity of experimentation necessary to make and use any immunogenic agent (i.e. peptide immunogen, nucleic acid immunogen and/or non-pathogenic organism) without known structural limitations for said activity; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to same; the complex nature of the invention; the state of the art which teaches the safety concerns regarding bacterial/viral vectors and cytokine adjuvants; and the breadth of the claims which fail to recite the limitations regarding administered immunogenic agents to produce the claimed activity, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58, 59, 61, 62, 67-75 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 58, 59, 61, 62, 67-74 are indefinite because of the recitation, "autologous immunogenic agent". The specification fails to teach the definition of an autologous immunogenic agent. Thus the metes and bounds of this claim cannot be determined.

Claim 69 is indefinite for the following reasons. Claim 69 recites, "the method according to any one of claims 62 or 68 wherein said immunogenic agent is presented to the immune system of said subject as a peptide immunogen, a nucleic acid immunogen and/or a non-pathogenic organism". Both claims 62 and 68 recite, "..wherein said immunogenic agent is an OPGL polypeptide..". Claim 69 is indefinite because it is unclear if the nucleic acid immunogen recited in claim 69 is a nucleic acid encoding OPGL polypeptide. It is unclear if the non-pathogenic organism recited in claim 69 comprises an OPGL polypeptide.

Claim 72 is indefinite because of the recitation, "wherein said non-pathogenic organism is bacterium at least one member selected from the group consisting of..". The instant claim is indefinite because vaccinia and pox virus are not bacterium. In addition, claim 72 is indefinite because it is not clear if the non-pathogenic organisms (i.e. bacterium and viruses) are transformed with a vector comprising a nucleic acid or not.

Claim 73 is indefinite because of the recitation, "RIBI" and "fab". Because the terms are abbreviated, it is unclear if these are protein, chemicals, analogs, etc.

Claim Objections

Claim 72 is objected to because of the following informalities: "bacterium" is misspelled. "vaccinia" is misspelled. Appropriate correction is required.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

RMD
5/8/08